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# Inner Ear Conundrum / Can a Stanford team of six scientists imported from Harvard cure deafness with stem cells?

By **Sam Whiting**

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Photo: CHRISTINA KOCI HERNANDEZ

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CHRISTINA KOCI HERNANDEZ/CHRONICLE (L to R) Sabina Mann, Stefan Heller, Christian Grimm, Kazou Oshima and Dawn Teo. Stefan Heller has started a Otolaryngology lab at Stanford University School of Medicine. Heller, 40, discovered

stem cells in the hair cells of the ear that may one day lead to a cure for deafness. This occurred at Harvard, then Stanford stole away Heller, his wife Sabine, also a scientist and their entire lab crew of 6. None are Americans. They have all new equipment set up at Stanford and are working on their experiments. They are a disheveled group. Heller the director, wears a t-shirt and Converse low tops around the lab. Please get a portrait of the group. Ask them not to dress different than any other lab day. They were given jackets that say "Stanford Otolaryngology" so maybe get that in picture. Also try to get some kind of science shot as secondary art. He has caterpillar cells mixing in giant beakers and a whole freezer full of DNA samples they brought out in a Fed Ex regrid

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It wasn't long after Stefan Heller discovered stem cells in the inner ear that he heard from the Stanford [University](#) School of Medicine.

Already at Harvard, Heller said he was uninterested in leaving. That's where the negotiation starts for Stanford. To poach Heller from Harvard took hiring his entire posse of six scientists, and outfitting a lab -- a \$500,000 investment. Plus there was the freezer full of DNA samples and cells trucked west at minus 80 degrees Celsius. The team was issued rental housing at the Stanford West complex across a field from the hospital, and black jackets to keep them warm on the bike ride, stitched with the red logo "Stanford Otolaryngology, Head and Neck Surgery."

Otolaryngology, which deals with diseases of the ear, larynx and upper respiratory system, is a new department at Stanford, and the chairman went into the medical marketplace like the general manager of the Yankees. Heller was pursued as the starting pitcher, or to put it in his native German, "like a soccer star," he says with a modest laugh.

"Harvard tried to keep me there as well," he says. "They gave me an endowed associate professorship which means hard money support. But Stanford matched all these things."

Heller describes the breakthrough that started the bidding as if it were no big deal. "We found stem cells that are potentially capable of regenerating hearing, which was

before that not known," he says. "That was sort of what made our lab famous in Boston."

At 40, Heller is the captain of an international team that includes two Berliners and one each from Auckland, New Zealand; Osaka, Japan; Bern, Switzerland; Singapore; and Shanghai. There are two from the Rhineland and they went to high school together -- Heller and his office manager Sabine Mann, who doubles as his wife. It was Mann who had the weakness for the California dream, but Heller who had to shovel the driveway, which was 200 yards long. On a recruiting trip, Heller noticed that everything at Stanford was contained in one medical campus, unlike Harvard, which is spread among the congestion of Boston.

"It's not easy driving. You don't find a parking spot. So the whole city of Boston is not good for a young researcher like me who seeks interaction," he says. "I liked that about Stanford. You can walk to talks. Then my post-docs get exposure to these things."

None of them had been exposed to the American interior so they caravanned out in European style, Heller and Mann and their two dogs in the lead Audi. After a mysterious breakdown in the ghost town of Bodie, they arrived en masse in early October.

It has taken him two months to get assembled in the Fairchild Building -- a low laboratory facility on the west side of the big hospital. Bunking with the neurobiologists until a new space is renovated, the otolaryngologists aren't hard to find among all the open doors in the second floor hallway. Theirs is the room where they speak "too much German," Heller admits. Even the Asians have picked up German, though they plan to soften it by adding an American researcher from Rockville, Md., next month.

The door is marked room D222 but inside it looks like "Room 222" of the '70s high school show. Heller sets the dress code in a Dunkin' Donuts T-shirt, scruffy jeans and low-top Converse All Stars.

On this day he is finally starting his first experiment -- growing inner ear cells in a culture dish, to test the new equipment -- and already people in the medical school

are asking, "When are the first transplantations taking place?" he says. "I'm a little careful of that, because we have to do animals first."

He wouldn't be here answering this question at all if he hadn't found stem cells in the vestibular organ, which controls balance. Both balance and hearing are controlled by hair cells. When the hearing cells are damaged by illness or noise, they die off and don't come back. A University of Virginia study 15 years ago found that cells in the vestibule have shown a small and limited ability to regenerate. Heller took that further and within these cells was able to isolate stem cells that continuously multiply. In culture dishes, these regenerative balance cells can be engineered to produce hearing cells.

The logical next step would be to transplant these into the auditory canal. "The problem with any surgical approach to the ear is you have the potential of doing more damage than you can do any good," he says. "So I don't think this will be successful any time soon."

That means 10 years and 10,000 mice, maybe more of each. The immediate future is drugs.

They can be tested directly on embryonic inner ear cells to see if any lead to over-production of hair cells. If a drug could be found that stimulates enough productivity within the damaged ear, this drug could be applied to a deaf ear. These can then be tested on animals, starting in a year or so.

"Anything out there costs \$2 a shot, he says. "As soon as we scale it up to 100,000 compounds and in triplicate, we're talking a lot of money. Stanford is supportive of that."

Keller's dream is to "find a drug that is effective, and it turns out to be a cheap drug that when applied to a deaf person will bring back hearing." That patent would return Stanford's investment.

"As far as I know nobody else is doing this. It isn't secretive," he says. "I'm openly talking to you."

His and Mann's other dream is to buy a house and they've already learned that bidding wars can cut both ways. They put in an offer on an Eichler knockoff in South Palo Alto, but got outgunned by a buyer offering all cash.

So they are still tenants in the university-owned town across Sand Hill Road. The scientists who work in a row in room D222 and another lab, also live, more or, less in a row. So do they get together nights and weekends to talk otolaryngology?

"In the hot tub," Heller says, smiling. "Ya."